

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board

Paper No. 29

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte CHI-HUEY WONG and CHUN-HUNG LIN

Appeal No. 1996-1959
Application No. 07/946,546

ON BRIEF

Before WINTERS, MILLS, and GRIMES, Administrative Patent Judges.

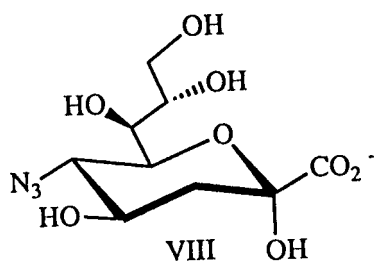
WINTERS, Administrative Patent Judge.

DECISION ON APPEAL

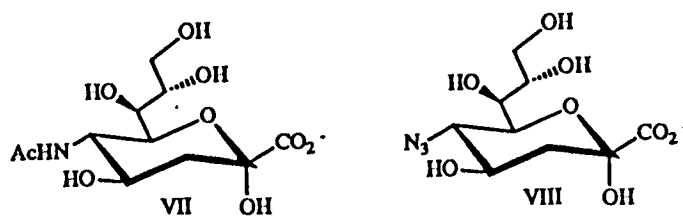
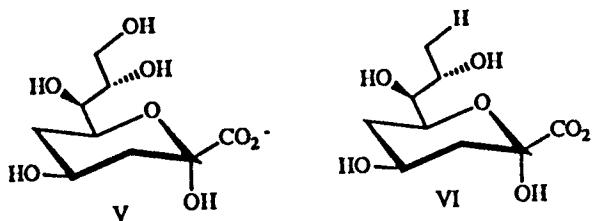
This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's final rejection of claims 3-6, 10-14 and 16 under 35 U.S.C. § 103(a) and the rejection of claim 6 under 35 U.S.C. § 102(b), all of the claims remaining in the application.

Claims 6 and 10 are representative and read as follows:

6. A compound of the Formula VIII:



10. A process of synthesizing a compound of the Formula V, VI, VII or VIII, below:



comprising the steps of:

(a) admixing in an aqueous solvent pyruvate, in the presence of a catalytic amount of sialic acid aldolase, with an acceptor substrate 2-deoxy-L-glucose, 2-deoxy-L-rhamnose, N-acetyl-L-mannosamine or 2-azido-2-deoxy-L-mannose, respectively, to form a reaction mixture; and

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(b) maintaining said reaction mixture for a time period and under biological reaction conditions sufficient for condensation of said pyruvate with said acceptor substrate and formation of a compound of Formula V, VI, VII or VIII.

The Examiner relies on the following references:

Schreiner et al. (Schreiner), "A Convenient Approach to 3-Deoxy-D-glycero-D-galacto-nonulosonic Acid (KDN), 5-Azido-5-deoxy-KDN and 5-Deoxy-KDN, and Their 4-Methylumbelliferyl 2a-Glycosides," Liebigs Ann. Chem. pp. 581-586 (1990)

Schrell et al. (Schrell), "Synthesis of the α -Methyl Ketoside of 5-Amino Neuraminic Acid Methyl Ester and Its corresponding 5-Myristoyl and 5-Cyclopropanoyl Derivative," Liebigs Ann. Chem. pp. 1111-1114 (1990)

Claim 6 stands rejected under 35 U.S.C. § 102(b) as anticipated by Schreiner.

Claim 6 stands rejected under 35 U.S.C. § 102(b) as anticipated by Schrell.

Claims 3-6, 10-14 and 16 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Schreiner in combination with Schrell.

We reverse.

BACKGROUND

Because of the stereoselectivity of enzymes such as aldolases that participate in the metabolism of carbohydrates, it is extremely difficult to design and make new carbohydrates that can be used to study carbohydrate metabolism. There is a need for such synthetic compounds for use as experimental tools in elucidating the molecular character of the numerous and varied pathways involved in carbohydrate anabolism and catabolism.

Of particular relevance to the present invention is the sugar, N-acetylneuraminic acid (NeuAc) or sialic acid. NeuAc is an integral component of most cells and is believed to play a major role in imparting electrical charge characteristics to such cells. Further, NeuAc-like

compounds such as the eight and nine-carbon sugar moieties KDO and KDN are major constituents of non-mammalian tissues.

N-Acetylneuraminic Acid (NeuAc) aldolase, also commonly referred to as sialic acid aldolase is a type I aldolase known to form an enamine intermediate with pyruvate, which reversibly reacts with the second substrate N-acetylmannosamine to give NeuAc...

Neu-Ac aldolase is known to accept many aldoses as acceptor substrates. In all previously known aldol condensation reactions with such acceptor substrates, the enamine [sic] intermediate approaches the si face of the incoming aldehyde substrate to form a new stereogenic center of S configuration....

Based on such current knowledge concerning aldolase stereoselectivity, therefore, NeuAc aldolase is considered to be useful for only the production of S-sugars having S configuration. As is disclosed hereinafter, NeuAc aldolase has now unexpectedly been found to be capable of the production of certain ketoaldonic acids having a formed stereogenic center of R configuration.

Specification, page 2, line 26 to page 3, line 35.

N-Acetylneuraminic acid (NeuAc) aldolase, is known to accept many aldoses as acceptor substrates to form stereogenic centers of S configuration. Despite the recognized stereoselectivity of NeuAc aldolase, Appellants have found that it is possible to produce ketoaldonic acids having a formed stereogenic center of R configuration when NeuAc aldolase catalyzes the condensation of pyruvate and certain five or six carbon L-configured acceptor substrate aldoses (Id., page 4 and page 9, lines 7-14). The compounds of the present claims have a formed stereogenic center of R configuration created by the re attack of pyruvate on the

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acceptor substrate. This is in contrast to previously known aldol condensation reactions using NeuAc aldolase where:

the attack is on the si face of the acceptor substrate and the resulting condensation product has a formed stereogenic center of S configuration. See e.g., Auge et al., New J. Chem., 12:733 (1988); Auge et al., Tetrahedron, 46:201 (1990); and Kim et al., J. Am. Chem. Soc., 110:6481 (1988).

Id., page 8, lines 21-27.

DISCUSSION

Anticipation

The rejections of claim 6 under 35 U.S.C. §102(b) will be addressed together, because Schreiner's compound 5e and Schrell's compound 3 are identical.

The Examiner argues that compound 5e in Scheme 3 of Schreiner (page 583) and compound 3 disclosed by Schrell (page 1111) illustrate the acid form of the compound designated Formula VIII of the present claim (Examiner's Answer, page 6, bottom, to the top of page 7). The Examiner points to Schreiner, page 583, column 1, lines 28-30 and argues that the dehydrogenated form of formula 5e was known in the art. According to the Examiner, the scheme depicted on page 1111 in Schrell also indicates that "[d]ehydrogenation of ketoaldonic acid compounds was previously known in this art," Id., page 7, first full paragraph. In the Supplemental

Answer, page 3, line 13 through page 4, line 4, the Examiner reiterates her position that the cited prior art anticipates claim 6 because both references disclose dehydrogenated forms of ketoaldonic acids.

Appellants argue that the compounds of the cited prior art and of claim 6, are isomers, "but not merely optical isomers" (Brief, page 2, bottom). At page 4 of the Brief, Appellants illustrate the claimed compound (VIIIa, on the left) and the prior art compound (3a, on the right). Comparison of substituent groups at a number of carbon atoms of these compounds reveals that they are in opposite configuration, (α or β). This observation is summarized in the table found at the bottom of page 4 of the Brief. The Reply Brief, page 6, discusses the same point, and illustrates an alternative chair form of compound of VIII (VIIIb) in which the oxygen is placed in the same position as the oxygen of the compound taught by both Schreiner and Schrell to allow easier comparison between the two formulae. Comparing the substituents of VIIIb and 5e, again, Appellants argue that at a number of carbon atoms, the substituents occupy different positions in the two molecules.

The discussion at page 4 of the Reply Brief respecting Exhibits 1 and 3 (which illustrate the conventional nomenclature and numbering of carbohydrates) addresses the significance of the positioning of substituents:

[t]hose structures represent glucose as compared to galactose, mannose, idose, allose, altrose, talose, or gulose because of the projections of the hydroxyls above or below the plane of the depicted ring. In galactose,

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the 4-position hydroxyl is up rather than down, where as in mannose, the 2-position hydroxyl is up rather than down, with all of the other hydroxyls maintaining the their same configurations relative to the plane of the ring.....by using ring structural formulas, workers of less than ordinary skill in the art can know the identity of a sugar, and one can identify a single sugar from among the 32 possible optical and anomeric isomers for a given $C_6H_{12}O_6$ sugar.

Appellants argue that the compound taught by Schreiner and Schrell differs from the compound of claim 6 with respect to the position of the substituent at a number of carbon atoms on the ring. According to the Appellants, just as glucose is different from galactose and mannose (by virtue of the positioning of the hydroxyl substituents), so too is the claimed compound different from that taught by the cited art.

The Examiner does not come to grips with Appellants' argument, either in the Answer or in the Supplemental Answer. Rather, the Examiner steadfastly maintains her position that the compound of the claim and that of the prior art are the same. The Examiner appears to ignore Appellants' exhibits, documenting conventional numbering and nomenclature for carbohydrates (sugars, in particular). In the face of Appellants' detailed comparison between the claimed compound and the prior art compound, including a discussion on the fundamentals of carbohydrate structure and nomenclature, we find that the Examiner's position is untenable.

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As stated in Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987), “[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” In addition, “...elements must be arranged as required by the claim” (In re Bond, 910 F.2d 831, 832, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990)). That is not the case here. On the contrary, the Examiner has not established that Schreiner or Schrell teaches the same compound recited in claim 6. The Examiner has not established a prima facie case of anticipation and, accordingly, the rejection of claim 6 under 35 U.S.C. § 102(b) as described by either Schreiner or Schrell is reversed.

Obviousness

The Examiner rejected claims 3-6, 10-14 and 16 under 35 U.S.C.

§ 103(a) over the combination of Schreiner and Schrell:

Schreiner et al show the acid form of the compound designated Formula VIII in instant claim 6 and instant claim 10...Schreiner et al also show a comparable method for the synthesis of the ketoaldonic acids. Note page 581-583. Further, Schreiner et al teach a method for the preparation of nonulosonic acid. Note pages 581 and 583. Thus, Schreiner et al substantially teach the present invention except for showing each compound and process step claimed...Regarding the compounds designated as Formulae V, VI, VII and IX described in instant claims 3-5 and 16, Schrell et al show closely analogous compounds that can contain suitable substituents, viz., “Ac”....With respect to instant process claims 11-15, Schrell et al show comparable process or method steps for the synthesis of closely analogous ketoaldonic acid compounds...Therefore it would have been obvious...to provide the ketoaldonic acid compounds described in the present invention

along with the process for preparing these ketoaldonic acid compounds because to modify the conventional ketoaldonic acid compounds shown by Schreiner et al and Schrell et al through dehydrogenation in order to obtain the desired compounds claimed was suggested earlier since Schreiner et al teach that comparison of the rate of hydrogenation in ketoaldonic isomers was previously known in this art and the Schrell et al teaching implies that the dehydrogenated form of the ketoaldonic compounds were also known in this art.

Answer, pages 4-6.

The Examiner does not explain, however, why the method steps of the references are considered “comparable” to the methods of the present claims. It appears that this rejection stems from the Examiner’s unwavering (and incorrect) position that the compound illustrated by Schreiner and Schrell (designated 5e and 3, respectively) is merely an acid form of the compound of Formula VIII (Claim 6). That position is incorrect, for the reasons already discussed. Further, the Examiner does not explain how the combined teachings of the references would have led the ordinary artisan to the specific compounds of claims 3-6 and 16, but simply opines that Schrell teaches compounds that are “analogous” to those of the present claims (Answer, first complete sentence, page 5 and the sentence bridging pages 4 and 5 of the Supplemental Answer).

With respect to method claims 10-14, the Examiner does not point to any portion or portions of the cited references disclosing or suggesting the limitations of those claims. Neither Schreiner nor Schrell teaches enzymatic (biochemical)

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reactions comprising pyruvate, NeuAc aldolase (sialic acid aldolase) and specific acceptor substrates. Neither reference teaches that the conventional stereoselectivity of NeuAc aldolase (sialic acid aldolase) can be “overridden” by use of specific acceptor substrates, resulting in aldol condensation products (ketoaldonic acids) with formed stereogenic centers of R configuration. Therefore, it is not clear how, and the Examiner has not explained how, the combination of references would lead the ordinary artisan to the claimed methods involving pyruvate, sialic acid aldolase and specific acceptor substrates. Accordingly, we reverse the rejection of claims 3-6, 10-14 and 16 over the combination of Schreiner and Schrell.

In conclusion, we reverse the rejection of claim 6 under 35 U.S.C.

§ 102(b) as anticipated by Schreiner; the rejection of claim 6 under 35 U.S.C.

§ 102(b) as being anticipated by Schrell; and the rejection of claims 3-6, 10-14 and 16 under 35 U.S.C. § 103(a) as unpatentable over Schreiner in combination with Schrell.

The Examiner’s decision is reversed.

REVERSE

SHERMAN D. WINTERS)

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DEMETRA J. MILLS)	
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